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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
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EXAMINER

GUPTA, ANISH

ART UNIT	PAPER NUMBER
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1654

DATE MAILED: 12/08/2003

81

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary

Application No.

09/822,965

Applicant(s)

INNERARITY ET AL.

Examiner

Anish Gupta

Art Unit

1654

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).
- Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

- 1) ☐ Responsive to communication(s) filed on ____.
- 2a) ☐ This action is FINAL. 2b) ☒ This action is non-final.
- 3) ☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

- 4) ☒ Claim(s) 14 and 18-20 is/are pending in the application.
- 4a) Of the above claim(s) ____ is/are withdrawn from consideration.
- 5) ☐ Claim(s) ____ is/are allowed.
- 6) ☒ Claim(s) 14 and 18-20 is/are rejected.
- 7) ☐ Claim(s) ____ is/are objected to.
- 8) ☐ Claim(s) ____ are subject to restriction and/or election requirement.

Application Papers

- 9) ☐ The specification is objected to by the Examiner.
- 10) ☐ The drawing(s) filed on ____ is/are: a) ☐ accepted or b) ☐ objected to by the Examiner.
Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).
- 11) ☐ The proposed drawing correction filed on ____ is: a) ☐ approved b) ☐ disapproved by the Examiner.
If approved, corrected drawings are required in reply to this Office action.
- 12) ☐ The oath or declaration is objected to by the Examiner.

Priority under 35 U.S.C. §§ 119 and 120

- 13) ☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).
a) ☐ All b) ☐ Some * c) ☐ None of:
1. ☐ Certified copies of the priority documents have been received.
2. ☐ Certified copies of the priority documents have been received in Application No. ____.
3. ☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).
* See the attached detailed Office action for a list of the certified copies not received.
- 14) ☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. § 119(e) (to a provisional application).
a) ☐ The translation of the foreign language provisional application has been received.
- 15) ☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. §§ 120 and/or 121.

Attachment(s)

- 1) ☒ Notice of References Cited (PTO-892) 4) ☐ Interview Summary (PTO-413) Paper No(s). ____
- 2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948) 5) ☐ Notice of Informal Patent Application (PTO-152)
- 3) ☒ Information Disclosure Statement(s) (PTO-1449) Paper No(s) 3 6) ☐ Other:

DETAILED ACTION

Amendments

The amendment filed 9-6-02 has been entered in part. The amendment to page 18, line 14-17, page 37 line 24-page 38 line 3, page 39-40, page 44-45, and page 45, line 13-22 has not been entered since the amendment contained the wrong page and line numbers. The page and line numbers do not correspond to the section that Applicants requested to have amended. Applicants are requested to resubmit the amendment with the appropriate page and line numbers.

The amendment to claims, filed 3-29-01 and 9-2-02 have been entered. Claims 14, 19, and 20 were amended and claims 1-13, 15-17, 21-28 were canceled in the 3-29-01 amendment. Claim 18 was amended in the 9-2-02 amendment. Claims 14, 18-20 are pending in this application.

Claim Objections

1. Claim 18 is objected to because of the following informalities: In the claim, Applicants recite K336E mutation. Applicants are requested to state "wherein mutation is at position 3363 and the lysine residue is substituted by glutamic acid residue" or the like.

Appropriate correction is required.

Specification

2. The disclosure is objected to because of the following informalities:

The MPEP, under 37 CFR 1.821(d), requires that "reference must be made to the sequence by use of the sequence identifier, preceded by "SEQ ID NO: " in the text of the description or claims. . ." On pages 17, 36, 38, of the specification, the sequences recited do not contain sequence identifiers.

Appropriate correction is required.

Claim Rejections - 35 USC § 112

The following is a quotation of the second paragraph of 35 U.S.C. 112:

The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

1. Claims 14, 18 and 20 is rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

In reviewing a claim for compliance with 35 U.S.C. § 112, second paragraph, the examiner must consider the claim as a whole to determine whether the claim apprises one of ordinary skill in the art of its scope and, therefore, serves the notice function required by 35 U.S.C. § 112, second paragraph by providing clear warning to others as to what constitutes infringement of the patent. See *Solomon v. Kimberly-Clark Corp.*, 216 F.3d 1372, 1379, 55 USPQ2d 1279, 1283 (Fed. Cir. 2000). If the language of the claim is such that a person of ordinary skill in the art could not interpret the metes and bounds of the claim so as to understand how to avoid infringement, a rejection of the claim under 35 U.S.C. § 112, second paragraph would be appropriate. See *Morton Int'l, Inc. v. Cardinal Chemical Co.*, 5 F.3d 1464, 1470, 28 USPQ2d 1190, 1195 (Fed. Cir. 1993).

Here, claim 14 state apo-B100 protein comprising a proteoglycan receptor mutation in site B. However, it is unclear what apo-B100 sequence must the mutated sequence be compared against. That is, the apo-B100 sequence exists in numerous organisms including Pig, rabbit, rat, hamster, mouse, hamster and chicken. All have differing amino acid sequences in the Site B, 3359-3369.

Art Unit: 1654

Thus, it is unclear which amino acid sequence is intended. One of ordinary skill in the art could not interpret the metes and bounds of the claims to understand how to avoid infringement.

In claim 18, the claim recites that the mutation is in site B and the amino acid sequence from position 3358 to 3359. Disclosed in the claim is a sequence from 3358 to 3359. It is unclear if the claims is drawn to only a di-peptide of 3358-3359, a decapeptide of 3358-3367, or a 12-amino acid sequence of 3358-3369. The 12 amino acid is included in the group since the site B mutation is defined to be from 3359-3369. Thus, it is unclear which amino acid sequence is claimed.

Claim Rejections - 35 USC § 101

35 U.S.C. 101 reads as follows:

Whoever invents or discovers any new and useful process, machine, manufacture, or composition of matter, or any new and useful improvement thereof, may obtain a patent therefor, subject to the conditions and requirements of this title.

1. Claims 14 and 20 are rejected under 35 U.S.C. 101 because the claimed invention is directed to non-statutory subject matter.

The claims are drawn to a Apo-B100 protein comprising a proteoglycan receptor mutation in Site B. It should be noted that numerous organisms have differing amino acids in the Site B relative to the human apo-B100. For example, Law et al. teach Hamster apo sequence that has the sequence SRLTRKRGLK in position 3359-3367 (see page 1114 of Law et al.). This sequence meet the claimed limitation of claims 14 since the 3359 Serine residue is different than the 3359 Threonine residue of human apo-B100. Further, it is known in the art that major classes of protein found in plasma are VLDL, IDL, LDL, and HDL. LDL's possess a core composed almost entirely cholesteryl esters and has a surface coat containing only apo B100 (see for example US 5914311). Note that the specification states that an LDL particle contains an apo-B100 and a lipid core which

Art Unit: 1654

is predominantly cholesteryl ester (see page 15). However, since the LDL's are found in the plasma of numerous animals, including hamster, and the claim does not state isolated or purified, the claimed product would qualify as a product of nature and hence non-statutory subject matter.

Claim Rejections - 35 USC § 102

The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

A person shall be entitled to a patent unless –

(b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

2. Claims 14 and 19 are rejected under 35 U.S.C. 102(b) as being anticipated by Law et al. (J. Lipid Research).

The claims are drawn to a Apo-B100 protein comprising a proteoglycan receptor mutation in Site B. Site B is defined as position *about* 3359 to *about* 3369. The claims also state that the site B is flanked on at least one side by contiguous sequence of at least 10 amino acids which is directly adjacent to site B in the wild type human apo-B100 sequence. The rejection assumes that apo-B100 is human apo-B100.

The reference discloses numerous apo-B100 sequence that have sequences that have mutations in site B when compared to the human apo-B100 (see page 1114). For example, the reference discloses a rabbit apo-b sequence, which has the sequence SSLTRKRGLKLA in position 3358-3359 (see page 1114). The human apo-b sequence in this range is TRLTRKRGLKL. Note that rabbit apo-b contains two different amino acids in positions 3358 and 3359. The instant specification a mutant of apo-B100 involve substitutions of four amino acid positions, 3363, 3362,

Art Unit: 1654

3364 and 3359 (see page 17). Since the reference discloses a mutation in position 3359, the reference meets all of the limitations of claim 14.

The reference also discloses rat, hamster, mouse, chicken and pig which would qualify as apo-B100 mutation as explained above and meet the limitations of the claim (see page 1114). The Pig sequence disclosed is SLMRKRGGL in positions 3359-3367 (see page 1114). Note that 3359 and 3361 differ from the native human apo-B100 and therefore would qualify as mutations in these position with respect to human apo-B100. The reference also states that region B of the apo-B100 is from 3359-3367 (see page 1109 and 1110). This amino acid range is within the "about" range recited on page 15 of the specification. Note that about allows for some variance as per MPEP 2144.05. In addition, the reference discloses that in the Pig sequence fragment 3368-3378 has an identical homology with the human apo-B100 (see page 1114). Therefore, the reference anticipates claim 19, since the reference discloses a sequence that contains mutations in site B and has at least 10 amino acids flanked to Site B that is directly adjacent to site B in the wild type human apo-B100 sequence.

3. Claims 14 and 20 are rejected under 35 U.S.C. 102(b) as being anticipated by Leroy et al. (J. Lipid Research) and Law et al. (J. of Lipid Research).

The claims are drawn to a Apo-B100 protein comprising a proteinglycan receptor mutation in Site B. Site B is defined as position *about* 3359 to *about* 3369. The claims also state that the site B is flanked on at least one side by contiguous sequence of at least 10 amino acids which is directly adjacent to site B in the wild type human apo-B100 sequence. The rejection assumes that apo-B100 is human apo-B100.

Art Unit: 1654

The reference discloses the isolation of rabbit LDL from plasma (see page 890). The isolation of LDL meets the limitation of claim 20, LDL particles. This is because, it is known in the art that major classes of protein found in plasma, similar to humans, are VLDL, IDL, LDL, and HDL. The LDL's possess a core composed almost entirely cholesteryl esters and has a surface coat containing only apo B100 (see for example US 5914311, col. 2). The instant application states that the LDL particle contains an apolipoprotein, such as apo-B100 and an cholesteryl ester (see page 15). The isolation of LDL from rabbit plasma would necessarily contain apo-B100 and cholesteryl ester.

Note that Law et al. teaches that rabbit apo-b100 sequence, which has the sequence SLTRKRGLKLA in position 3359-3369 (see page 1114). The human apo-b sequence in this range is TRLTRKRGLKL. Note that rabbit apo-b100 contains two different amino acids in positions 3358 and 3359. The instant specification a mutant of apo-B100 involve substitutions of four amino acid positions, 3363, 3362, 3364 and 3359 (see page 17). Since the reference discloses a mutation in position 3359, the reference meets all of the limitations of claim 14.

Here, the reference of Law has been applied to "Show that a characteristic not disclosed in the reference is inherent," i.e. the sequence.

4. The reference of Barenholz et al. (US 5914311) has been cited to show the state of the art with respect to LDL and their compositions.


5. Any inquiry concerning this communication or earlier communications from the examiner should be directed to Anish Gupta whose telephone number is (703) 308-4001. If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Brenda Brumback, can normally be reached on (703)306-3220. The fax phone number of this group is (703) 308-4242.

Application/Control Number: 09/822,965

Page 8

Art Unit: 1654

Any inquiry of a general nature or relating to the status of this application should be directed to the Group receptionist whose telephone number is (703) 308-0196.

 12/1/03
Anish Gupta